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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STUCKER, JEFFREY J	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 04/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/659,324	SORENSEN, BIRGER	
	Examiner	Art Unit	
	Jeffrey Stucker	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-33,35,37-45,47 and 49-66* is/are pending in the application.

4a) Of the above claim(s) *16-33,35,37-44 and 62-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45,47 and 49-52* is/are rejected.

7)☒ Claim(s) *45,47,49-61,65 and 66* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/11/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This Office Action is in response to the Election filed 3/13/06. Claims 16-33, 35, 37-45, 47, 49-66 are pending. Claims 16-33, 35, 37-44, and 62-64 are withdrawn from consideration as being drawn to non-elected inventions. Claims 45, 47, 49-61, 65, and 66 are objected to and claims 45, 47, 49-52 are rejected

Applicant's election with traverse of Group II, generic SEQ ID NO: 15, and specific sequence SEQ ID NO:18 in the reply filed on 3/13/06 is acknowledged. The traversal is on the grounds that Groups I and II are closely related and that a search of the claims of one Group would likely include a search of the other claims of the other Group and that all of the claims can be searched simultaneously and a that a duplicative search with possibly inconsistent results may occur if the restriction is maintained.

This is not found persuasive because the Groups are directed to products and methods, and as set forth in the Restriction Requirement, the products can be used in materially different processes. The searches of each Group may overlap but would not be co-extensive. Thus, Applicant may not be getting a full, complete, search if both Groups were examined together and the quality of the search may suffer and Applicant might not get the quality of examination that Applicant's single application

fees paid for. Applicant's concern in regards to the uniformity of searching is misplaced. The Office strives for uniformity in prosecution, and it is the position of the Office that all of the instant claims cannot be examined in one application without undue burden on the Office for the reasons set forth in the Restriction Requirement.

Applicant further argues that each of the independent claims requires the use of "at least one peptide..." and that the Examiner seems to indicate that only one SEQ ID NO will be examined in this application and that this is allegedly inconsistent with the MPEP because "normally ten sequences" is a reasonable number and that none of the factors listed in § 803.04 as necessitating a reduction in the number of sequences that may be reasonably examined are present in SEQ ID NOs:16-20. Applicant notes that only five sequences are recited in the quoted Markush group and that these sequences are all related in that they are all ultimate species of SEQ ID NO:15 and that applicant is entitled to a search and that this would not constitute an unreasonable burden on the Examiner.

This is not found persuasive because the section of the MPEP quoted in Applicant's response is directed to nucleic acid sequences. The only reference to amino acid sequences is the

statement quoted by Applicant that "In some exceptional cases, the complex nature of the claimed material, for example a protein amino acid sequence reciting three dimensional folds, may necessitate that the reasonable number of sequences to be selected be less than ten." This is only an example, not an exhaustive list. Given that each of the sequences has different amino acids and that the individual amino acids contribute to and influence the tertiary structure of the resulting peptide, it would be readily apparent that each peptide is going to have a distinct structure different from each of the other amino acid sequences. Applicant has not specifically disclosed what substantial structural feature is common to the sequences that is essential to a common disclosed utility. There is no showing, evidence, or statement that each of the sequences would be obvious over the others. The search of each sequence is not coextensive and to fully search and examine each would constitute an undue burden on the Office. It is noted that SEQ ID NO:15 has been deleted from the claims. The claims will be examined to the extent that they read on SEQ ID NO:18.

The requirement is still deemed proper and is therefore made FINAL.

The specification is objected to for the following informalities:

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2), see pages 4-6. However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 because it does not appear that the sequences set forth on pages 4-6 were included in the required CRF and paper copy. Full compliance is required in response to this Office Action. Failure to do so will be considered to be nonresponsive and could result in ABANDONMENT of the instant application.

The specification is objected to for failing to adhere to the requirements of the sequence rules. Applicant must append SEQ ID Nos. to all mentions of specific sequences in the specification. See 37 CFR § 1.821(d).

The specification is further objected to for numerous informalities. For example, at page 1, line 23, the ";" should be "," and page 2, line 8, "resent" should be "recent". Other such minor errors abound in the specification. Applicant is urged to carefully review the specification and correct such errors.

Appropriate correction is required.

Claims 45, 47, 49-61, 65, and 66 are objected to for containing non-elected subject matter.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 53-61, 65, and 66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18,

24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (BdPatAppInt 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

The claims are directed to a "pharmaceutical composition for stimulating the immune system of a human." The specification discloses that Applicant's invention is intended to be an "effective prophylactic and therapeutic vaccine" (page 3, lines 28-31; an "active principle of a prophylactic or therapeutic vaccine intended to provide protection against [HIV-1]" (page 21, lines 26-30). The "pharmaceutical composition" appears from the specification to be intended to be equivalent to a vaccine for preventing or treating HIV-1 infection.

It is well known in the art that retroviral infections in general, and HIV infections in particular, are refractory to anti-viral therapies. The obstacles to therapy of HIV are well documented in the literature. These obstacles include: 1) the extensive genomic diversity and mutation rate associated with the HIV retrovirus, particularly with respect to the gene encoding the envelope protein; 2) the fact that the modes of viral transmission include both virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert manner, as well as via free virus transmission; 3) the existence of a latent form of the virus; 4) the ability of the virus to evade immune responses in the central nervous system due to the blood-brain barrier; and 5) the complexity and variation of the pathology of HIV infection in different individuals. The existence of these obstacles establish that the contemporary knowledge in the art would not allow one skilled in the art to use the claimed invention with a reasonable expectation of success and without undue experimentation. Further, it is well known in the art that individuals infected with HIV produce neutralizing antibodies to the virus, yet these antibodies are not protective and do not prevent the infection from progressing to its lethal conclusion. The failure of all immune-system-boosting therapies for treating AIDS is discussed

by Fox. Thus, it is clear from the evidence of Fox, that the ability to treat and/or prevent HIV infection is highly unpredictable and has met with very little success.

The instant invention is drawn to a pharmaceutical composition comprising SEQ ID NO:18 intended to stimulate the immune system of a human but the specification does not sufficiently support the full scope of the claims. The term "pharmaceutical composition", in this context is a vaccine, implies a preparation intended for active immunological prophylaxis; e.g., preparations of killed microbes of virulent strains or living microbes of attenuated (variant or mutant) strains; or microbial, fungal, plant, protozoa, or metazoan derivatives or products. Although nearly any protein when inoculated can cause an immune reaction, the prophylactic nature of this reaction is not guaranteed and has to be experimentally determined. Prophylaxis is defined as the prevention of disease or of a process that can lead to disease. For example, the *Illustrated Dictionary of Immunology* defines vaccine as a composition that stimulates protective antibodies and T cell immunity and induces active immunity. Paul in *Fundamental Immunology* teaches that vaccines were developed primarily as a prophylactic measure to prevent disease. This is achieved by use of an antigenic (immunogenic) agent to actively stimulate the

immune system to reduce the number of carriers of a disease and to prevent others from contracting the disease. Testing protocols are designed to test the efficacy of the vaccines which include challenge trials or natural exposure to the disease agent in an endemic area. Further, he teaches that there is not always a correlation between seroconversion and protection from disease. Given the teachings in the art, it is clear that a compound that merely induces an immune response is not sufficient but must be protective to qualify as a vaccine. See at the top of page 1312: "[T]here was not always a correlation between seroconversion and protection from disease...."

The ability of a vaccine to raise a protective immune response depends on the structure of the protein epitopes. Paul teaches that to determine the immunogenicity of certain regions of a protein, knowledge of the three dimensional structure of the protein is required to determine which polypeptides in a given protein would be accessible on the surface of the protein in order for the putative antigenic determinant to be bound by the antibody. In addition, Paul states that mobility of the putative antigenic determinant within the native protein structure is also a determining factor for the binding of the antigenic determinant to an antibody. Paul points out (page 250,

lines 4-8) that "Measurement of the mobility in the native protein is largely dependent on the availability of a high resolution crystal structure, so its applicability is limited to only a small subset of proteins." Riffkin et al. (*Gene*, 1995) teaches that a single amino acid change can alter the structure of the protein dramatically. Abaza et al. (*J. of Protein Chemistry*, 1992) teaches that mutations outside of the antigenic epitope exert an effect on the structure of the epitope. Because the structure of the protein determines its antigenicity and thereby its function as a vaccine, these structures cannot be predicted. In regards to the factors cited in the lack of utility rejection, Cohen et al. recognize other problems: "No vaccine capable of eliciting protective immunity to HIV infection has been formulated. HIV presents a formidable challenge to immune surveillance based on many factors, including hypervariability of its principal neutralizing domain (V3) (19), concealment of critical, functional domains in the external envelope glycoprotein (gp120) behind inessential structures (20), and infection of APCs resulting in their dysfunction (21). Substantial progress has been made recently in defining neutralizing domains within the HIV envelope, and in augmenting the immune response to HIV proteins (22). Despite these important advances, an effective HIV vaccine remains

elusive, we propose, because the immediate immunodeficiency accompanying HIV infection creates another obstacle to a successful vaccine (23)." Applicant's specification does not address these factors and does not disclose that the instant invention has overcome these problems.

The specification discloses some specific sequences and teaches how to synthesize them by conventional means. SEQ ID NO:18 was apparently synthesized (examples 11 and 14) and injected into rodents to ascertain safety (example 16). None of these examples provides support for the scope of the claims.

Applicant has not provided any convincing evidence that the claimed pharmaceutical composition is indeed enabled for preventing or treating HIV-1 infection and have not provided sufficient guidance to allow one skilled in the art to practice the claimed invention with a reasonable expectation of success and without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

Given the uncertainty in the vaccine art as demonstrated by the references and the lack of working examples in the instant specification, the instant application is not enabled for vaccines or methods of vaccinating. The instant invention, based

on the evidence as a whole, in light of the factors articulated by the court in *In re Wands*, lacks an enabling disclosure.

SEQ ID NO:18 is free of the art of record.

No claims are allowable.

Papers related this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

The Group 1600 Official Fax number is: (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Stucker whose telephone number is (571)-272-0911. The examiner can normally be reached Monday to Thursday from 7:00am-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (571)-272-0902.

JEFFREY STUCKER
PRIMARY EXAMINER